UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,898	11/28/2000	Leroy Hood	P-IS 4403	7808

41552 7590 03/11/2005

MCDERMOTT, WILL & EMERY
4370 LA JOLLA VILLAGE DRIVE, SUITE 700
SAN DIEGO, CA 92122

EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,898	HOOD ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-32,58-65,70,95-104 and 135-153* is/are pending in the application.

4a) Of the above claim(s) *17-32,58-64,135-137,140,142 and 143* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-16,65,70-80,90,95-104,138,139,141 and 144-153* is/are rejected.

7)☒ Claim(s) *10,12,14,74,76,78,98,100 and 102* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/18/2004 has been entered.

Claims 1, 6-32, 58-65, 70-80, 90, 95-104, and 135-153 are pending.

Claims 2-5, 33-57, 66-69, 81-89, 91-94, and 105-134 are cancelled.

Claims 17-32, 58-64, 135-137, 140, and 142-143 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 6-16, 65, 70-80, 90, 95-104, 138-139, 141, and 144-153 presently are under examination.

Information Disclosure Statement

IDS filed 12/20/2004 has been considered by the examiner.

Claim Objections

Claims 10, 12, 14, 74, 76, 78, 98, 100, and 102 are objected to because of the following informalities: claims 10, 12, and 14 improperly depend from cancelled claim 5; claims 74, 76, and 78 improperly depend from cancelled claim 69; claims 98, 100, and 102 improperly depend from cancelled claim 94.

Claim Rejections - 35 USC § 101

Non-statutory Subject Matter

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 6-9, 11, 13, and 15-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 6-9, 11, 13, and 15-16 are directed to a method for determining a comparative expression profile. "However, not all processes are statutory under 35 U.S.C. 101." *See* MPEP § 2106. The disclosed method does not recite physical steps to be performed in order to achieve the goal of the method. Step (a) of the claimed method is not limited to a physical step, and all other steps are merely those of data manipulation. The method does not actually transform a set of data, but only recite statistical manipulations.

When a computer-implemented method does not recite a physical step or an actual transformation of data, it may be statutory when the claimed invention as a whole accomplishes a practical application. "That is, it must produce a useful, concrete and tangible result." *See* MPEP § 2106. In the instant case, the result of the method is the determination whether a multidimensional coordinate point is within or outside of a reference expression region. The claims do not recite tangible expression of the determination, nor any recitation of an actual (*i.e.*, concrete) result in a form useful to one skilled in the art. Thus, the method does not recite steps of producing something that is concrete, useful, and tangible, and is not statutory. It is noted that claims 65, 70-73, 75, 77-80, 90, 95-97, 99, 101, 103-104, and 144-153, while directed to

methods similar to that of claim 1, recite physical steps of determining expression levels of a sample and/or contacting a specimen with a target, and therefore are statutory.

Claim Rejections - 35 USC § 112, first paragraph

Enablement Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-16, 65, 70-80, 90, 95-104, 138-139, 141, and 144-153 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

An applicants' argument in the response filed 11/16/2004 stating that the claimed methods are sufficiently enabled by the teaching in the specification is found not persuasive.

Applicants state that the method of the invention can be used to diagnose the health state or disease state of an individual by comparing expression levels of molecules in diseased and healthy reference individuals. (Applicant's response filed 11/16/2004, p. 14). Applicants also state that the specification teaches various methods for determining the health state of an individual. *Id.*

In order to practice the method, one of skill in the art has to know which individual is healthy and which is not (*i.e.*, what expression levels of molecules are indicative of healthy and

diseases individuals). In order to correlate a health expression level with a disease level , one needs to know relevant genes or molecules associated with the disease. Also, to practice the invention, one has to know how to determine expression levels, *i.e.*, what type of an assay/method to use (DNA/RNA probe assay, protein assay, antibody assay, etc.) or how to create probes, antibodies, or other target molecules to test a diseased stage. For example, applicants describe a target on p. 31-32 and state that the target has characteristics useful for binding molecules of a specimen. The specification further discloses that the target can contain any molecule, *i.e.*, nucleic acid, polypeptide, antibodies, etc. *Id.* Therefore, to create "a target," one has to know either nature of the target or at least what type of changes one is going to detect. The specification does not provide working examples for diagnosing health or disease stages of a particular disease. The analysis of prior art (as it is shown in the prior office actions filed 7/3/2003 and 3/16/2004) shows that a large amount of inventive discovery and work would be required to make comparative expression profiling for diagnosis and there is no large body of knowledge from which one could have drawn ideas how to identify diseases stage of an individual. The specification only provides for a general idea that one needs to compare expression levels of health and disease stages and that a reference expression level might be verified by statistical methods. These statements are only a wish and a challenge for a future research, not an invention. Further undue experimentation is required to practice the instant invention without any information about diseases, genes, molecules involved, types of assay or probes, or other information connecting disease to expression levels. This constitutes undue experimentation. For these reasons and those previously set forth, the rejection is maintained.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-9, 11, 13, 15-16, 65, 70-73, 75, 77, 79-80, 90, 95-97, 99, 101, 103-104, 138-139, 141, 144-153 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the independent claims, 1, 65, 90, 138, 141, and 144, the metes and bounds of the step comparing expression levels with a reference expression region is not clear. One skilled in the art would not know how to compare expression levels (*i.e.*, specific numbers) with an expression region without specific directions as to how to perform the comparison and "parameters" are to be compared. Applicant arguments in the response filed 11/16/2004 are found not persuasive. Applicant did not particularly point to a definition of "comparing" or any specific example in the specification supporting the applicant's argument that "one skilled in the art would readily understand the meaning of "comparing." (Applicant's response filed 11/16/2004, p. 13).

35 U.S.C. 112 ¶2 rejection of claims 1, 6-9, 11, 13, 15-16, 65, 70-73, 75, 77, 79-80, 90, 95-97, 99, 101, 103-104, 138-139, 141, 144-153 is hereby withdrawn. Examiner agrees with applicants that the meaning "determining" is readily understood by one skilled in the art.

Claims 10, 12, 14, 74, 76, 78, 98, 100, and 102 recite the limitation "said target." There is insufficient antecedent basis for this limitation in the claims. It is unclear what limitations, if any, of a parent claim is intended, therefore the claims are indefinite. As the limitation intended is

unclear, and no parental claim recites any "target," these claims are not further treated on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6-8, 11, 13, 15-16, 65, 70-72, 75, 77, 79-80, 90, 95-96, 99, 101, 103-104, 138-139, and 141 are rejected under 35 U.S.C. 102(e) as being anticipated by Friend, U.S. Patent 6,324,479, for the reasons of record as set forth in the previous Office action dated 3/16/2004, as applied to claims 1-16, 65, 70-90, 95-104, 138, 139, 141, and 143-153.

Friend discloses methods, a computer system, and a computer-readable medium for determining activity levels of health and disease stages using gene expression profiles, *see* fig. 3 and Sections 5.2 and 5.3. Steps of Friend's methods (determining expression levels; comparing the levels, and determining a disease stage) are similar to that of the instant claims. Thus, Friend anticipates instant claims 1, 6-8, 11, 13, 15-16, 65, 70-72, 75, 77, 79-80, 90, 95-96, 99, 101, 103-104, 138-139, and 141.

Applicants' arguments in the response and declaration filed 11/16/2004 have been carefully considered, but failed to persuade the examiner of error in determination of anticipation.

In particular, applicants argue that Friend discloses a "unidirectional analysis" in contrast to a multidimentional analysis of the instant claims. The examiner notes that multidimentional coordinate points are recited only in instant claims 1, 6-16, 138-139, and 141. Thus, applicants' arguments are moot with regard to claims 65, 70-73, 75, 77, 79-80, 90, 95-97, 99, 101, 103-104, 138-139, 141, 144-153, and the examiner maintains that Friend anticipates these claims. Applicants provide an explanation and examples illustrating the differences between Friend's method and the method of instant claim 1. It is recognized that the instant method and Friend's method produce different results. However, particular statistical methods used in applicants' examples to show differences are not reflected in instant claim 1. Results of Friend's method are graphically presented on fig. 1-2, and 4. It is clear that the results are two-dimensional, not unidimensional, and are within the scope of instant claim 1. For these reasons, the rejection is maintained.

Claims 1, 6-8, 11, 13, 15-16, 65, 70-72, 75, 77, 79-80, 90, 95-96, 99, 101, 103-104, 138-139, and 141 are rejected under 35 U.S.C. 102(e) as being anticipated by Friend, U.S.2001/0018182, for the reasons of record as set forth in the previous Office action dated 3/16/2004, as applied to claims 1-16, 65, 70-90, 95-104, 138, 139, 141, and 143-153.

Friend discloses methods, a computer system, and a computer-readable medium for determining activity levels of health and disease stages using gene expression profiles, *see* and

Sections 5.2 and 5.3. Steps of Friend's methods (determining expression levels; comparing the levels, and determining a disease stage) are similar to that of the instant claims. Thus, Friend anticipates instant claims 1, 6-8, 11, 13, 15-16, 65, 70-72, 75, 77, 79-80, 90, 95-96, 99, 101, 103-104, 138-139, and 141.

Applicants' arguments in the response and declaration filed 11/16/2004 have been carefully considered, but failed to persuade the examiner of error in determination of anticipation for the same reasons as those set forth above, therefore the rejection is maintained..

Claims 1, 6-16, 65, 70-80, 90, 95-104, 138-139, 141, and 144-153 are rejected under 35 U.S.C. 102(b) as being anticipated by Prashar, WO 99/57130.

Prashar discloses a process to study changes in gene expression profile, similar to that of the instant claims. Steps of the method of instant claims 1, 65, 90, and 144 are generally disclosed in claim 19 and Example 1 in Prashar's publication. Prashar discloses a three-dimensional graphical representation of gene expression (fig. 2 a-c), thus anticipating claim 1. Prashar compares health and disease stages of T lymphocytes, examples 1-14, thus anticipating instant claims 6-8, 70-72, 95-96, and 145-146. Prashar discloses a sample as being blood (p. 15), thus anticipating claims 9, 73, 97, and 144. Prashar discloses a sample as being nucleic acid (p. 35), thus anticipating claims 11, 75, 99, and 148. Prashar discloses reporting expression profiles (fig. 1-2), thus anticipating claims 16, 80, 104, and 153. Prashar discloses a specimen comprising T lymphocytes that are activated by a small molecule (example 1, line 25-27), thus anticipating claims 15, 79, 103, and 152. Prashar discloses a target comprising nucleic acids (p. 16), thus anticipating claim 149.

Prashar discloses a computer system, similar to that of instant claims 138-139. Prashar discloses that expression data may be compared with corresponding relevant data that has been stored in an electronic or computer-readable format (p. 5, line 15-24) and uses computer-accessible databases (p. 6 and table 4-5) such as GeneBank for determining and comparing expression data, thus anticipating claims 138-139 and 141. Prashar discloses a target-array (p. 22, line 3-12), thus anticipating claim 147.

Claims 65, 70-72, 75, 77, 80, 90, 95-96, 99, 101, and 104 are rejected under 35 U.S.C. 102(a) as being anticipated by Levine, U.S. Patent 6,02,135.

Levine discloses a method for diagnosing disease, similar to instant claims 65, 70-72, 75, 77, 80, 90, 95-96, 99, 101, and 104. Steps of the method of instant claims 65 and 90 (determining expression levels; comparing the levels, and determining a disease stage) are disclosed in Example, col.7-8. Thus, Levine anticipates claims 65 and 90. Levine discloses a reference expression profile (col.1, line 30-39), thus anticipating claim 70. Levine discloses a perturbed expression profile indicative of a disease (col. 1, line 41-45), thus anticipating claims 71-72 and 95-96. Levine discloses a sample as being a nucleic acid or a polypeptide (col. 1, line48-52), thus anticipates claims 75, 77, 99, and 101. Levine discloses reporting of expression profiles (fig. 1-2), thus anticipating claims 80 and 104.

Claims 1, 6-9, 11, 13, 15-16, 65, 70-73, 75, 77, 79-80, 90, 95-97, 99, 101, 103-104, 138-139, 141, 144-149, and 152-153 are rejected under 35 U.S.C. 102(a) as being anticipated by Bao, U.S. Patent 6,251,601.

Bao discloses a method similar to that of instant claims 1, 65, 90, and 144. Steps of the method (as recited in rejections above) are discloses in col. 3 and sections (9) Array Hybridization and (10) Array Detection. Thus, Bao anticipates claims 65 and 90. Bao discloses a multidimensional expression point (fig. 2), thus anticipating claim 1. Bao discloses a sample as being blood (col. 11, line 59) or lymphatic system cells (col. 11, line 64 and col. 24, line 42-46), thus anticipating claim 9, 73, 97, and 144. Bao discloses comparing a sample expression with a reference expression (col. 16, line 15-56), thus anticipating claims 6-8, 70-72, 95-96, and 145-146. Bao discloses a sample as being nucleic acids (col. 3, line 3-6), thus anticipating claims 11, 75, 99, and 148. Bao discloses that multiple gene expression at the protein level also can be examined by the use of "microdot" immunoassays, which are two-dimensional arrays of immobilized antigens on a substrate (col. 2, line 9-11), thus anticipating claims 13, 77, 101, and 150. Bao discloses a labeled sample molecules (col. 6), thus anticipating claims15, 79, 103, and 152. Bao discloses reporting expression levels (col. 16, line 57-66), thus anticipating claims 16, 80, 104, and 153. Bao discloses a computer system and a computer readable medium comprising a processor, a memory, and a comparative profiler (col. 15, line 58-65 and col. 16, line 45-65-col. 17, line 1-20), thus anticipating claims 138-139 and 141. Bao discloses a DNA array (col. 25, line 41), thus anticipating claims 147 and 149.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Feber, U.S. Patent 6,774,120 (disclosing a method of determining expression levels).

2. Cohen, U.S. Patent 6,346,381 (disclosing a method of detecting expression levels in nucleic acid samples).

3. Leethanakul, Oncogene, 19:3220-24 (2000) (disclosing a method of determining distinct patterns of differential gene expression).

4. Hughes, Cell, 102:109-126 (July 7, 2000) (disclosing multidimentional expression profiles).

5. Cole, Nature Genetics Supplement, 21:38-41 (Jan. 1999) (disclosing a 3D model for presenting expression data obtained by using microarrays).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on M-F 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MM

MARJORIE MORAN
PATENT EXAMINER
Marjorie A. Moran
2/17/05